

Docket No.: 000166.0108-US01  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
J. Michael Ramstack et al.

Application No.: 10/022,859

Group Art Unit: 1615

Filed: December 20, 2001

Examiner: A. E. Pulliam

For: **PREPARATION OF MICROPARTICLES  
HAVING IMPROVED FLOWABILITY**

**TRANSMITTAL LETTER**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed are the following items for filing in connection with the above-referenced Patent Application:

1. Fee Transmittal;
2. Petition for Extension of Time under 37 CFR 1.136(a) (in duplicate);
3. Amendment Transmittal Letter (in duplicate);
4. Amendment in Response to Non-Final Office Action;
5. Declaration of J. Michael Ramstack, Ph.D. under 37 CFR 1.132;
6. Copy of the return receipt postcard filed and date-stamped by U.S. Patent and Trademark Office on August 28, 2002;
7. Copy of the return receipt postcard filed and date-stamped by the U.S. Patent and Trademark Office on July 31, 2003;

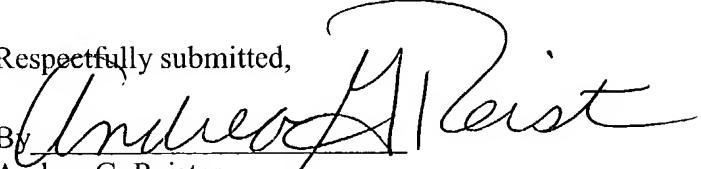
8. Second Supplemental Information Disclosure Statement;
9. Form F CO/SB/08a/b;
10. Two cited documents;
11. Check No. 326644 for \$462.00 to cover:  
\$180.00 IDS submission fee;  
\$110.00 one-month extension of time fee;  
\$172.00 additional claims fee; and
12. Return receipt postcard.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-0740, under Docket No. 000166.0108-US01. A duplicate copy of this paper is enclosed.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-0740.

Dated: March 31, 2004

Respectfully submitted,

By   
Andrea G. Reister

Registration No.: 36,253  
COVINGTON & BURLING  
1201 Pennsylvania Avenue, N.W.  
Washington, DC 20004-2401  
(202) 662-6000



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ramstack *et al.*  
Appl. No.: 10/022,859  
Filed: December 20, 2001  
For: **Preparation of Microparticles  
Having Improved Flowability**

Art Unit: 1615  
Examiner: Amy E. Pulliam  
Atty. Docket: 00166.0108.US01

**Declaration of J. Michael Ramstack, Ph.D.  
Under 37 C.F.R. § 1.132**

Commissioner for Patents  
Washington, D.C. 20231

I, J. Michael Ramstack, Ph.D., hereby declare and state as follows.

1. I have a B.S. degree in Mechanical Engineering, an M.S. degree in Biomedical Engineering, and a Ph.D. degree in Chemical Engineering. I have over twenty years experience in biotechnology, medical device, and pharmaceutical industries. I am currently employed by Alkermes, Inc. ("Alkermes") as a Senior Development Engineer. I have been employed by Alkermes or their predecessor in business for more than ten years. The above-captioned U.S. Patent Application No. 10/022,859 ("the '859 application") is owned by Alkermes Controlled Therapeutics Inc. II, a subsidiary of Alkermes.

2. I have read and understood the '859 application. I am a co-inventor of the invention disclosed and described in the '859 application.

3. I understand that the Office Action dated December 1, 2003 in the '859 application asserts that "it is within the knowledge of the ordinary artisan that increased dryness equals increased flowability." The data presented in the '859 application are contrary to the assertion that increased dryness equals increased flowability. In particular, Batch E that appears

in Table 3 on page 16 of the '859 application illustrates that increased dryness cannot be equated with increased flowability. As noted in Table 3, the angle of repose of the Batch E placebo microparticles after being in a closed container at room temperature for three years was 19.1°. The Batch E microparticles were then subjected to 24 hours under vacuum, which increased their dryness. After being subjected to further drying under vacuum, the angle of repose increased to 26.5°, a decrease in flowability. The Batch E microparticles demonstrate that increased dryness can lead to decreased flowability.

4. That increased dryness cannot be equated with increased flowability is also demonstrated by Batch F in Table 3 on page 16 of the '859 application. As noted on page 15, lines 16-28 and in Table 3 on page 16 of the '859 application, the Batch F microparticles were conditioned in accordance with the present invention by maintaining them at 25 °C for at least five days. The conditioned Batch F microparticles had an angle of repose of 19.7°. The Batch F microparticles were then subjected to 24 hours under vacuum, which increased their dryness. After being subjected to further drying under vacuum, the angle of repose increased to 24.1°, a decrease in flowability. Like the Batch E microparticles, the Batch F microparticles demonstrate that increased dryness can lead to decreased flowability. Moreover, the Batch F microparticles demonstrate that conditioning the microparticles is not the same as drying microparticles since the conditioned microparticles had better flowability than the microparticles after being further dried under vacuum.

5. On page 8 of the '859 application it is noted that microparticles can be prepared in accordance with, for example, U.S. Patent Nos. 5,650,173 and 5,654,008, and then be subjected to the conditioning process disclosed in the '859 application. I am a co-inventor of the invention

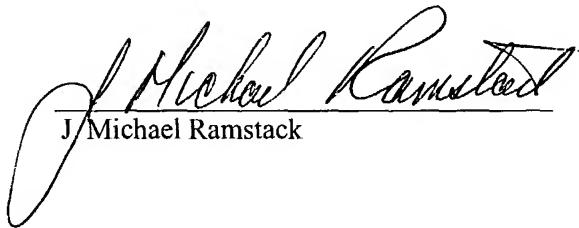
disclosed and described in U.S. Patent No. 5,650,173 ("the '173 patent"). I am familiar with and understand the subject matter of U.S. Patent No. 5,654,008 ("the '008 patent"), which is assigned to Alkermes Controlled Therapeutics Inc. II, through my work at Alkermes. The '173 and '008 patents disclose methods of preparing microparticles in which the microparticles are thoroughly dried. Through my work at Alkermes making microparticles using the methods disclosed in the '173 and '008 patents, it was discovered that the microparticles may exhibit poor flowability, even though the microparticles were thoroughly dried. The process disclosed and described in the '859 application was discovered as a way to improve the flowability of dry but poorly flowing microparticles.

6. I understand that the Office Action dated December 1, 2003 in the '859 application asserts that "it is within the ordinary skill of the pharmaceutical art to set aside a recently made batch of microparticles, allowing them to thoroughly dry, prior to using the microparticles in any further formulations." As explained in paragraph 5 above, even if microparticles are allowed to thoroughly dry, that alone is not a guarantee of good flowability. As explained in paragraphs 3 and 4, increased dryness cannot be equated with increased flowability, and conditioning the microparticles cannot be equated with drying the microparticles.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United

Applicants: Ramstack, *et al.*  
Appl. No.: 10/022,859

Sates Code and that such willful false statements may jeopardize the validity of the above-captioned patent application or any patent issued thereon.

  
J/Michael Ramstack

Date: 3-24-04



Date: August 28, 2002 Atty Docket No.: 000166.0108-US01

Inventor: J. Michael Ramstack, et al.

Application No.: 10/022,859 Filing Date: December 20,2001

Title: PREPARATION OF MICROPARTICLES HAVING IMPROVED FLOWABILITY

**Documents Filed:**

Transmittal Letter (in duplicate);

Fee Transmittal;

Amendment Transmittal Letter (in duplicate);

Preliminary Amendment;

Supplemental Information Disclosure Statement;

Form PTO/SB/08A;

One cited document;

Check No. 300679 for \$336.00 to cover the additional claims fee; and

**STAMP AND RETURN**

Return receipt postcard.



RECEIVED IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

VIA HAND CARRY TO: Examiner Amy Pulliam, United States Patent and Trademark Office, Group Art Unit 1615, Crystal Mall 1, 1911 South Clark Place, Arlington, VA 22202

Application No.: 10/022,859-Conf. #1415

Docket No.: 000166.0108-US01

Filed: December 20, 2001

Inventors: J. Michael Ramstack, Ph.D., *et al.*

For: Preparation of Microparticles Having Improved Flowability

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

1. Transmittal Letter (in duplicate);
2. Resubmission of Documents;
3. Copy of date-stamped postcard evidencing receipt by the PTO on August 28, 2002 of documents listed below as items 4-11;
4. Transmittal Letter;
5. Fee Transmittal;
6. Amendment Transmittal Letter;
7. Preliminary Amendment;
8. Supplemental Information Disclosure Statement;
9. Form PTO/SB/08A;
10. One cited document;
11. Check No. 300679 for \$336 to cover additional claim fee; and
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